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# Clinical significance of medial vs. lateral compartment patellofemoral osteoarthritis: cross-sectional analyses in an adult population with knee pain

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## ABSTRACT

### Objective

To determine the comparative prevalence, associations with selected patient characteristics and clinical outcomes of medial and lateral compartment patellofemoral joint (PFJ) osteoarthritis (OA).

### Methods

Information was collected by questionnaires, clinical assessment and x-rays from 745 eligible community-dwelling symptomatic adults aged ≥50 years. PFJ joint space narrowing (JSN) and osteophytes (OP) were scored from skyline radiographs using the OARSI atlas. Multilevel models were used to assess associations of compartmental PFJOA with age, gender, BMI and varus/valgus malalignment, while median regression was used to examine associations with clinical outcomes (current pain intensity 0-10NRS and WOMAC Function 0-68).

### Results

Isolated lateral PFJOA was more common than isolated medial PFJOA, particularly at higher severity thresholds. Irrespective of severity threshold, age (≥2:OR 1.19; 1.12, 1.26), BMI (≥2:OR 1.15; 1.07, 1.24) and valgus malalignment (≥2:OR 2.58; 1.09, 6.07) were associated with increased odds of isolated lateral JSN but isolated medial JSN was only associated with age (≥2:OR 1.20; 1.14, 1.27). The pattern of association was less clear for PFJ OP. Isolated lateral PFJOA, defined by JSN or OP, was associated with higher pain scores than isolated medial but these differences were modest and non-significant. A similar pattern of association was seen for functional limitation but only when PFJOA was defined by JSN.

### Conclusions

Isolated lateral PFJOA is more common than isolated medial and it is more consistently associated with established OA risk factors. It is also associated with higher, but clinically non-significant, pain and function scores than isolated medial PFJOA, particularly when defined using JSN.

**SIGNIFICANCE AND INNOVATIONS**

- We show that while mild patellofemoral osteoarthritis is equally common in both compartments of the joint, moderate to severe disease more commonly affects the lateral compartment.
- Isolated lateral PFJOA is associated with higher pain and function scores than isolated medial PFJOA, but these differences are only modest and clinically non-significant. We further show that the relationship between compartmental radiographic PFJOA and clinical outcomes may vary depending on the morphological feature and severity threshold used to define PFJOA.
- Our findings support the call for better patient selection for clinical trials, for example, through the inclusion of symptomatic patients with probable PFJ narrowing (JSN grade ≥1), and possibly the need to rethink current PFJOA treatments that attempt to realign the patella medially

Patellofemoral joint (PFJ) osteoarthritis (OA) contributes to knee pain and functional limitation[1-3] and may be a target for early management of knee OA.[4] There is a lack of effective conservative management options for PFJOA with trials of bracing, taping and exercise yielding conflicting results.[5-8] These conservative treatment strategies, as well as some surgical treatments, largely attempt to realign the patella medially to unload the lateral PFJ compartment. This is because PFJOA is believed to be predominantly a disease of the lateral PFJ compartment based on the 'Law of Valgus' put forward by Ficat and Hungerford in their seminal work on the disorders of the PFJ.[9] The law suggests that the predominant frontal plane force acting on the patella during knee motion is directed laterally, leading to excessive loading of the lateral facet of the PFJ. This is in line with more recent biomechanical studies of the PFJ that report higher loading of the lateral PFJ facet[10-13] with the lateral facet contact force estimated to be 4 – 6 times higher than the medial facet contact force.[13]

However, higher prevalence of OA in the lateral PFJ compartment is not consistently found in epidemiological studies. In one of the earliest studies of 66 patients with relatively severe knee OA attending an orthopaedic clinic, lateral PFJ disease was found on plain radiography in 89% of knees, compared with only 11% of knees with medial PFJ disease.[14] Elahi et al included the dominant knees of 292 participants recruited from the community and showed that 67 out of 86 participants with patellofemoral OA had evidence of predominantly lateral PFJOA compared with 19 who had evidence of predominantly medial PFJOA.[15] In contrast, the higher frequency of lateral PFJOA observed in these studies was recently challenged by evidence from large-scale magnetic resonance imaging (MRI) studies of knee OA, which reported medial patellofemoral cartilage damage and bone marrow lesions (BMLs) at least as common as lateral.[16-19] (See **Supplementary Data Table S1**). However, the clinical significance of the MRI lesions in the medial PFJ compartment is unclear. Stefanik et al observed more common and more severe knee pain when OA involved the lateral PFJ compartment, despite the high prevalence of MRI detected cartilage damage in the medial PFJ compartment.[20]

Studies of risk factors for compartmental PFJOA have shown an association with patella dislocation or subluxation,[14] patella malalignment[21-23] and valgus-varus malalignment.[15,24] The established OA risk factors of age, gender and body mass index (BMI) have also been studied in relation to the PFJ[1,25] but the association of these risk factors with compartmental PFJOA has not been specifically assessed. Furthermore, the association of PFJOA with pain and functional limitation is now well-recognised but there is limited evidence about the relative contribution of compartmental PFJ disease to these outcomes.[20] Understanding the relative prevalence, association with risk factors and clinical significance of medial and lateral compartment PFJOA may lead to a better understanding of the aetiology of PFJOA and inform the development of treatment strategies as well as the design of clinical trials. Using cross-sectional baseline data from the Clinical Assessment Study of the Knee (CAS-K), a cohort of community-dwelling adults aged 50 years and over with knee pain, our aim was to determine the relative (a) frequency, (b) direction and magnitude of association with selected risk factors, and (c) the strength of association with pain and functional limitation of lateral versus medial PFJOA. We hypothesised that the findings depended on the morphological feature and severity threshold chosen and that this, therefore, might be one of the reasons for conflicting findings reported in previous studies.

## PATIENTS & METHODS

### *Study Population*

The Clinical Assessment Study of the Knee (CAS-K) is a prospective, population-based, observational cohort study of knee pain in adults aged ≥50 years. Individuals reporting knee pain in the last year were identified through a postal survey and invited to attend a research clinic where detailed clinical assessment and bilateral knee x-rays were performed. Details of the CAS-K cohort design, methods and recruitment are described

elsewhere.[26,27,] Ethical approval was obtained for all stages of the study and participants provided written informed consent.

### *Data collection*

*Definition of medial and lateral PFJOA using plain radiography*

Three views of the knee were obtained – a weight-bearing posteroanterior (PA) semiflexed,[28] skyline and lateral views. The lateral and skyline views were obtained in a supine position with the knees flexed to 45 degrees. The PA view and the posterior aspect of the lateral view were used to assess the tibiofemoral joint (TFJ) while the PFJ was assessed using the skyline view. Six radiographers who had been trained to standardize the x-rays performed all the imaging in one radiology department and regular quality control sessions were held.

A single reader, blinded to clinical and questionnaire data, scored all the study x-rays at baseline. Individual radiographic features on the PA and skyline views were scored using the Osteoarthritis Research Society International (OARSI) atlas.[29] Osteophytes (OP) on the posterior tibial surface do not appear in the atlas but were judged on the same basis of severity as other OP in the lateral view. There was good intraobserver and interobserver repeatability (Kappa = 0.46-0.86) for scores of individual radiographic features in the skyline views using the OARSI atlas. Further details of the radiographic scoring and definitions have been previously published.[30]

For each radiographic feature (JSN and OP), we classified the patellofemoral joint (irrespective of tibiofemoral joint involvement) into one of four mutually exclusive categories based on the pattern of compartmental involvement: 'isolated medial', 'isolated lateral', 'mixed medial and lateral', and 'neither medial nor lateral' ('Neither'). A sliding threshold definition of compartmental PFJOA was applied based on severity of individual radiographic features at grade ≥1 (mild), ≥2 (moderate) and ≥3 (severe). Radiographic severity of TFJOA was classified as none, mild, moderate or severe using a combined scoring system previously described.[31]

*Risk factors*

Age, gender and body mass index (BMI) were recorded at baseline. Frontal plane knee malalignment was assessed using the proxy clinical measurements of intercondylar and intermalleolar distances performed on standing. Varus and valgus malalignment were defined as intercondylar and intermalleolar distances >0cm respectively.

*Clinical outcomes*

Knee pain severity and self-reported functional limitation were studied. Data on pain was collected in clinic using the Chronic Pain Grade scale,[32] which included an 11-point numerical rating scale (NRS 0-10) for current knee pain intensity. Participants were asked to score the severity of pain in the index knee, which was identified by the participant as the more problematic knee or chosen at random where both knees were equally symptomatic. Patient-reported functional limitation was assessed using WOMAC LK3.0 Function subscale scores (0-68).[33]

*Statistical Analysis*

Firstly, we calculated the prevalence of compartmental PFJOA by radiographic feature using the sliding cut-off for severity threshold as described above. Subsequent analyses of association with selected patient characteristics and clinical outcomes were limited to thresholds grade ≥1 and ≥2 as there were insufficient numbers in the most severe category (JSN/OP grade 3) to run regression models. We then used *knee-level* (1475 knees) multilevel multinomial regression models taking into account the clustering of both knees in the same subject, to determine the associations between selected patient characteristics (age, gender, BMI, frontal plane knee malalignment) and compartmental PFJOA. Finally, quantile (median) regression models (performed at *person-level*

– 745 index knees) were used to assess the association between compartmental PFJOA and the clinical outcomes of pain and functional limitation, adjusting for age, gender, BMI and severity of TFJOA. We compared pain and function scores in each compartmental PFJOA category, and at each threshold, using the 'neither' category as reference.

## RESULTS

Of the 819 people who attended the research clinic for an assessment, 745 were eligible for the current analysis – 55% women; mean age (SD) 65.2 (8.6) years; BMI (SD) 29.6 (5.2) kg/m$^2$. Reasons for ineligibility were: no current or recent knee pain (32), participants declined radiography (2), existing diagnosis of inflammatory arthritis verified by medical records (16), total knee replacement (TKR) of index knee (15), unlabelled PA view (2), absent patella (2), skyline views considered uninterpretable (5). These 745 individuals contributed 1475 knees to the analysis (excluding 15 TKR of non-index knee).

*Relative frequency of compartmental radiographic PFJOA*

Using skyline JSN to define PFJOA, the prevalence of isolated medial PFJOA was similar to isolated lateral PFJOA at the mild (JSN ≥1) threshold but at the moderate (JSN≥2) and severe (JSN=3) thresholds isolated lateral PFJOA was more common than isolated medial PFJOA. When defined using skyline OP, the prevalence of isolated lateral PFJOA was higher than isolated medial PFJOA across all severity thresholds. (**Table 1**)

*Compartmental radiographic PFJOA: association with selected patient characteristics*

Multilevel multinomial regression analyses showed that irrespective of the severity threshold chosen, isolated lateral PFJOA, when defined by JSN, was associated with higher age (≥1: OR 1.15; 1.11, 1.20; ≥2: OR 1.19; 1.12, 1.26) and BMI (≥1: OR 1.15; 1.09, 1.22; ≥2: OR 1.15; 1.07, 1.24), and with valgus malalignment (≥1: OR 2.12; 1.07, 4.18; ≥2: OR 2.58; 1.09, 6.07) with varus malalignment appearing protective (≥1: OR 0.18; 0.07, 0.46; ≥2: OR 0.30; 0.09, 0.90) while isolated medial PFJOA was only associated with age (≥1: OR 1.12; 1.08, 1.17; ≥2: OR 1.20; 1.14, 1.27). When defined using OP, both isolated lateral PFJOA and isolated medial PFJOA were associated with higher age and BMI at both thresholds, while isolated medial PFJOA, but not isolated lateral PFJOA, was associated with varus malalignment at the moderate (≥2) threshold. Men in this cohort were found to have higher odds of PFJ OP than women, but this association was only seen at the mild (≥1) threshold. (**Table 2**)

*Compartmental radiographic PFJOA: association with clinical outcomes*

In quantile (median) regression, after adjusting for covariates, median pain scores for isolated lateral PFJOA were higher than those for isolated medial PFJOA whether defined by JSN or OP and irrespective of threshold. However, the difference in median pain intensity was generally less than 0.5 points on 0-10 NRS (**Figure 1**). When compared with knees with 'neither medial nor lateral' PFJOA, the difference in median pain intensity was only statistically significant for knees with 'mixed' compartmental PFJOA and only at the JSN grade ≥1 (p=0.006) and OP grade ≥2 (p=0.027) thresholds. (**Figure 1**)

In similar regression models but with WOMAC Function as the outcome, median function scores for isolated lateral PFJOA were higher than isolated medial PFJOA, but only when defined by JSN (**Figure 2**). The observed magnitude of difference was roughly 4-7 points on 0-68 scale. When compared with knees with 'neither medial nor lateral' PFJOA, the difference in median function scores was statistically significant for knees with isolated lateral PFJOA but only at the JSN grade ≥1 (p=0.012) threshold. (**Figure 2**)

## DISCUSSION

Our cross-sectional study using plain radiography in community-dwelling symptomatic adults suggests that isolated lateral PFJOA is more common than isolated medial PFJOA particularly at the higher severity thresholds, and is more consistently associated with established OA risk factors. Additionally, we show that the pattern of associations of compartmental PFJOA with selected risk factors and clinical outcomes differs depending on the morphological feature and severity threshold used to define PFJOA and we suspect that this may be one reason for the conflicting results of clinical trials to date.

The prevalence and risk factor associations of isolated medial and isolated lateral PFJOA varied depending on the radiographic feature (JSN vs. OP) and the severity threshold (mild, moderate or severe) chosen. Our finding of higher prevalence of moderate to severe PFJOA in the lateral compartment than the medial is consistent with other x-ray studies[14,15] but at variance with MRI studies, which demonstrate at least equal or even greater frequency of medial PFJ cartilage damage and bone marrow lesions (BMLs) than lateral.[16,20] Our results, however, further suggest a roughly equal frequency of isolated medial and isolated lateral JSN at the mild JSN (JSN ≥1) threshold. Cahue et al[24] showed that patellofemoral progression was more common in the lateral compartment than medial, and it could be that even though early PFJOA is equally common in both compartments the faster progression in the lateral compartment means that moderate to severe disease is more commonly found in the lateral PFJ compartment than medial. The variance of our results with MRI studies may simply reflect differences in the sensitivity of both imaging modalities as the frequency of lateral PFJ cartilage damage and BMLs on MRI was found to exceed the medial at the most severe thresholds.[16]

PFJOA is associated with the traditional OA risk factors of age, gender and BMI.[1,25] Our findings show that the association of PFJOA, whether defined by JSN or OP, with increasing age holds true for both compartments of the PFJ irrespective of severity threshold applied. With respect to gender, we found unexpected reduced odds of PFJ OP among symptomatic women at the mild (OP ≥1) threshold. Other investigators have not shown a gender difference in the risk of compartmental PFJOA[15] and indeed previous population based studies have found a higher prevalence of radiographic OA in women than in men.[34,35] A male preponderance of symptomatic OA in our cohort has been previously reported[36,37] and is thought to be due to selective non-participation of older symptomatic women and possibly differences in occupation between the men and women in our cohort[37]

At both severity thresholds used in this study, higher BMI and valgus malalignment were associated with higher odds of isolated lateral JSN, with varus malalignment appearing protective. Isolated medial JSN was only associated with age. The reason for this is not clear. A possible explanation is that different processes drive JSN in the medial and lateral PFJ compartments with lateral JSN being largely driven by load-related damage (BMI and malalignment) while medial JSN is more age-related degeneration, probably driven by a relative lack of loading, which could impair cartilage nutrition.[38,39] However, our finding of an association of isolated medial PFJ OP with load-related risk factors of BMI and varus malalignment (at ≥2 threshold) does not support the notion of a lack of loading of the medial PFJ compartment. Furthermore, in contrast to our results, Elahi et al[15] showed that lateral PFJ JSN was associated with valgus malalignment and medial PFJ JSN with varus malalignment but found no association between compartmental PFJ JSN and BMI. The absence of an association between varus malalignment and isolated medial JSN (at both thresholds) or isolated medial OP (at ≥1 threshold) in our study could partly reflect the imprecise nature of our measure of malalignment using intermalleolar and intercondylar distances compared to the full limb radiograph measures of alignment used by Elahi et al.[15] On the other hand, their finding of no association between compartmental PFJ JSN and BMI could be due to a lack of power given

the small sample size in their study (n = 86). Clearly, further studies are needed to elucidate the mechanisms underlying the development of medial and lateral PFJOA.

Stefanik et al,[20] showed that despite a high prevalence of MRI-detected cartilage damage in the medial PFJ compartment, knee pain was more common and more severe when OA was either isolated to or inclusive of the lateral PFJ compartment. In contrast, we found the highest pain scores in knees with 'mixed' compartmental PFJOA, and when compared with the 'neither' compartmental PFJOA category, the difference in median pain score was highest in knees with 'mixed' compartmental PFJOA. In the current study, knees with isolated lateral PFJOA, whether defined by JSN or OP, had higher median pain scores than knees with isolated medial PFJOA, but these differences were mostly modest (<0.5 on a 0-10 NRS) and clinically non-significant. A possible explanation for these findings is a lack of power in the current study to detect clinically meaningful differences in pain scores between isolated lateral and isolated medial PFJOA. However, if our findings are correct, they suggest a need to rethink current treatment strategies for PFJOA that attempt to realign the patella medially.

Furthermore, our results suggest that the relationship between compartmental radiographic PFJOA and clinical outcomes may vary depending on the morphological feature and severity threshold used to define PFJOA. These findings require confirmation in other x-ray based symptomatic PFJOA cohorts. If confirmed, we suspect that this could be one reason for the conflicting results of trials of conservative treatments for PFJOA to date. Trials have often recruited participants on the basis of definite osteophytes[5-7] or moderate JSN (JSN ≥2) in the PFJ[6] mostly excluding participants with probable narrowing in the PFJ (JSN ≥1). The results of the current study suggest that inclusion of symptomatic patients with probable PFJ narrowing might lead to better patient selection for clinical trials.

There are a number of limitations to our study. We did not collect data on patella malalignment, which is an important risk factor for PFJOA.[21] However, studies have found no association between patella malalignment and clinical symptoms,[21,42] and the absence of this data in our cohort is not likely to bias our conclusions about the clinical significance of compartmental PFJOA. Additionally, given the cross-sectional design of the current study, we are unable to comment on the temporality of the relationship between compartmental PFJOA and the clinical outcomes of pain and functional limitation.

## CONCLUSION

Our cross-sectional study using radiography in community-dwelling symptomatic adults suggests that isolated lateral PFJOA is more common than isolated medial, and more consistently associated with known OA risk factors. Isolated lateral PFJOA is associated with higher pain and function scores than isolated medial PFJOA, particularly when defined using JSN and not OP. These differences, however, were generally modest and clinically non-significant in the present study. Future longitudinal research should investigate the relative incidence and progression of lateral and medial PFJ compartmental disease and their determinants.

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**Table 1. Relative frequency of medial and lateral patellofemoral joint involvement from plain radiographs of 1475 knees (745 persons), by morphological feature and severity threshold (OARSI atlas)**

| | Severity threshold | | |
|---|---|---|---|
| | ≥1 | ≥2 | ≥3 |
| ***Morphological feature: Joint space narrowing (JSN)*** | | | |
| Neither medial nor lateral PFJ JSN | 935 *(63)* | 1184 *(80)* | 1303 *(88)* |
| Isolated medial PFJ JSN | 197 *(13)* | 97 *(7)* | 42 *(3)* |
| Isolated lateral PFJ JSN | 240 *(16)* | 162 *(11)* | 121 *(8)* |
| Mixed medial and lateral PFJ JSN | 103 *(7)* | 32 *(2)* | 9 *(1)* |
| ***Morphological feature: Osteophytes (OP)*** | | | |
| Neither medial nor lateral PFJ OP | 576 *(31)* | 1118 *(76)* | 1299 *(88)* |
| Isolated medial PFJ OP | 158 *(11)* | 105 *(7)* | 52 *(4)* |
| Isolated lateral PFJ OP | 286 *(19)* | 162 *(11)* | 101 *(7)* |
| Mixed medial and lateral PFJ OP | 455 *(31)* | 90 *(6)* | 23 *(2)* |

Figures are number (percentage) of knees. OP Osteophytes; JSN Joint Space Narrowing.

**Table 2. Risk factor associations (multilevel, multinomial regression analysis using data from 1475 knees from 745 participants)**

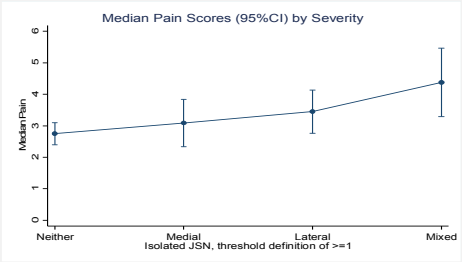
| | | JOINT SPACE NARROWING | | |
|---|---|---|---|---|
| | | **Threshold ≥1 (reference: neither medial nor lateral)** | | |
| | | Isolated medial | Isolated lateral | Mixed |
| | *Reference* | aOR (95%CI) | aOR (95%CI) | aOR (95%CI) |
| Age | *Per year* | **1.12 (1.08, 1.17)** | **1.15 (1.11, 1.20)** | **1.20 (1.15, 1.25)** |
| Female | *Male* | 1.06 (0.55, 2.02) | 0.76 (0.40, 1.43) | 1.15 (0.55, 2.39) |
| BMI | *per kg/m²* | 1.06 (0.99, 1.13) | **1.15 (1.09, 1.22)** | **1.14 (1.07, 1.22)** |
| Varus | *Neither* | 0.71 (0.31, 1.62) | **0.18 (0.07, 0.46)** | 0.90 (0.35, 2.27) |
| Valgus | *Neither* | 1.61 (0.80, 3.26) | **2.12 (1.07, 4.18)** | 2.18 (1.00, 4.74) |
| | | **Threshold ≥2 (reference: neither medial nor lateral)** | | |
| | | Isolated medial | Isolated lateral | Mixed |
| | *Reference* | aOR (95%CI) | aOR (95%CI) | aOR (95%CI) |
| Age | *Per year* | **1.20 (1.14, 1.27)** | **1.19 (1.12, 1.26)** | **1.23 (1.15, 1.32)** |
| Female | *Male* | 0.97 (0.41, 2.31) | 0.76 (0.34, 1.72) | 1.23 (0.42, 3.62) |
| BMI | *per kg/m²* | 1.01 (0.93, 1.10) | **1.15 (1.07, 1.24)** | 1.07 (0.97, 1.19) |
| Varus | *Neither* | 0.58 (0.19, 1.80) | **0.30 (0.09, 0.90)** | 0.65 (0.16, 2.58) |
| Valgus | *Neither* | 2.49 (0.99, 6.24) | **2.58 (1.09, 6.07)** | 1.60 (0.50, 5.09) |
| | | **OSTEOPHYTES** | | |
| | | **Threshold ≥1 (reference: neither medial nor lateral)** | | |
| | | Isolated medial | Isolated lateral | Mixed |
| | *Reference* | aOR (95%CI) | aOR (95%CI) | aOR (95%CI) |
| Age | *Per year* | **1.13 (1.08, 1.19)** | **1.15 (1.10, 1.20)** | **1.18 (1.12, 1.23)** |
| Female | *Male* | **0.31 (0.14, 0.70)** | **0.21 (0.09, 0.46)** | **0.25 (0.11, 0.53)** |
| BMI | *per kg/m²* | **1.25 (1.15, 1.36)** | **1.24 (1.14, 1.34)** | **1.34 (1.23, 1.45)** |
| Varus | *Neither* | 1.68 (0.63, 4.50) | 1.15 (0.44, 3.02) | 2.07 (0.81, 5.27) |
| Valgus | *Neither* | 1.00 (0.42, 2.40) | 2.25 (0.99, 5.11) | 1.43 (0.64, 3.22) |
| | | **Threshold ≥2 (reference: neither medial nor lateral)** | | |
| | | Isolated medial | Isolated lateral | Mixed |
| | *Reference* | aOR (95%CI) | aOR (95%CI) | aOR (95%CI) |
| Age | *Per year* | **1.22 (1.11, 1.35)** | **1.20 (1.09, 1.33)** | **1.22 (1.10, 1.35)** |
| Female | *Male* | 1.27 (0.50, 3.19) | 1.44 (0.60, 3.47) | 1.16 (0.45, 2.97) |
| BMI | *per kg/m²* | **1.31 (1.14, 1.50)** | **1.24 (1.08, 1.42)** | **1.32 (1.15, 1.51)** |
| Varus | *Neither* | **5.02 (1.53, 16.44)** | 1.87 (0.57, 6.12) | **3.69 (1.07, 12.75)** |
| Valgus | *Neither* | 1.10 (0.40, 3.05) | 2.25 (0.88, 5.76) | 2.40 (0.88, 6.57) |

aOR: adjusted odds ratio, adjusted for age, gender, BMI (Body Mass Index) and malalignment taking into account the clustering of knees within subjects. PFJ, Patellofemoral joint; OA, Osteoarthritis; CI, Confidence interval.

**Figure 1. Association of compartmental PFJOA with pain**

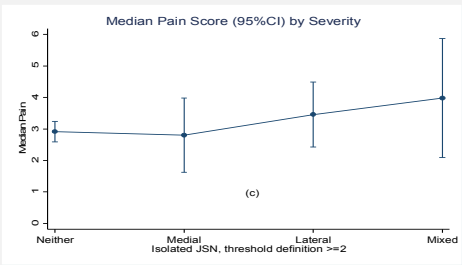
**JOINT SPACE NARROWING**

**Threshold ≥1**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median pain score (95%CI)** | 2.8 (2.4, 3.1) | 3.1 (2.3, 3.8) | 3.5 (2.8, 4.1) | **4.4 (3.3, 5.5)** |
| **Median difference (95%CI)** | Ref | 0.3 (-0.5, 1.2) | 0.7 (-0.1, 1.5) | **1.6 (0.5, 2.8)** |
| **P value** | - | P=0.419 | P=0.084 | **P=0.006** |

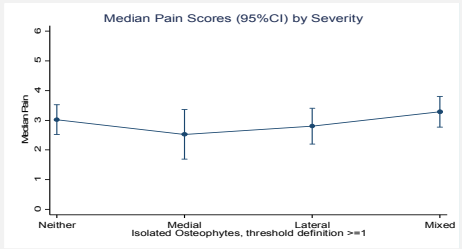
**Threshold ≥2**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median pain score (95%CI)** | 2.9 (2.6, 3.2) | 2.8 (1.6, 4.0) | 3.5 (2.4, 4.5) | 4.0 (2.1, 5.9) |
| **Median difference (95%CI)** | Ref | -0.1 (-1.3, 1.1) | 0.6 (-0.6, 1.7) | 1.1 (-0.9, 3.0) |
| **P value** | - | P=0.862 | P=0.343 | P=0.281 |

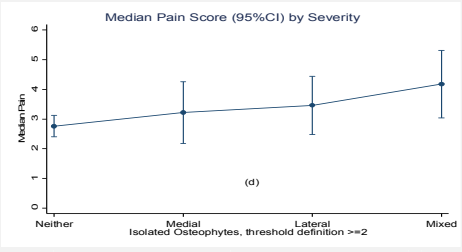
**OSTEOPHYTES**

**Threshold Grade ≥1**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median pain score (95%CI)** | 3.0 (2.5, 3.5) | 2.5 (1.7, 3.4) | 2.8 (2.2, 3.4) | 3.3 (2.8, 3.8) |
| **Median difference (95%CI)** | Ref | -0.5 (-1.5, 0.5) | -0.2 (-1.0, 0.6) | 0.3 (-0.5, 1.1) |
| **P value** | - | P=0.316 | P=0.599 | P=0.506 |

**Threshold Grade ≥2**



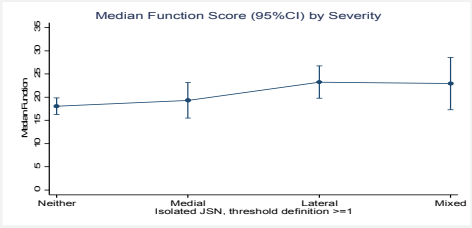

| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median pain score (95%CI)** | 2.8 (2.4, 3.1) | 3.2 (2.2, 4.3) | 3.5 (2.5, 4.4) | **4.2 (3.0, 5.3)** |
| **Median difference (95%CI)** | Ref | 0.5 (-0.7, 1.6) | 0.7 (-0.4, 1.8) | **1.4 (0.2, 2.7)** |
| **P value** | - | P=0.800 | P=0.207 | **P=0.027** |

aOR: adjusted odds ratio, adjusted for age, gender, BMI (Body Mass Index) and malalignment taking into account the clustering of knees within subjects. PFJ, Patellofemoral joint; OA, Osteoarthritis; CI, Confidence interval.

**Figure 2. Association of compartmental PFJOA with functional limitation**

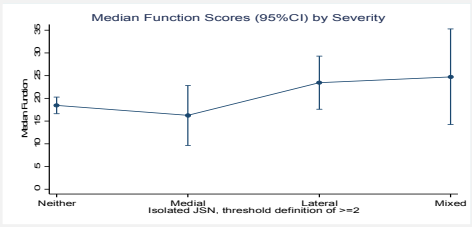
**JOINT SPACE NARROWING**

**Threshold ≥1**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median function score (95%CI)** | 18.1 (16.3, 19.8) | 19.3 (15.5, 23.2) | **23.2 (19.8, 26.7)** | 22.9 (17.3, 28.6) |
| **Median difference (95%CI)** | Ref | 1.3 (-3.0, 5.5) | **5.2 (1.1, 9.2)** | 4.9 (-1.2, 10.9) |
| **P value** | - | P=0.557 | **P=0.012** | P=0.114 |

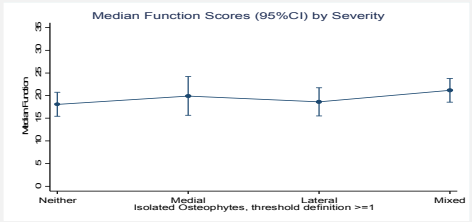
**Threshold ≥2**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median function score (95%CI)** | 18.5 (16.6, 20.3) | 16.3 (9.7, 22.9) | 23.5 (17.6, 29.4) | 24.8 (14.2, 35.3) |
| **Median difference (95%CI)** | Ref | -2.2 (-9.1, 4.7) | 5.0 (-1.4, 11.4) | 6.3 (-4.5, 17.1) |
| **P value** | - | P=0.531 | P=0.123 | P=0.254 |

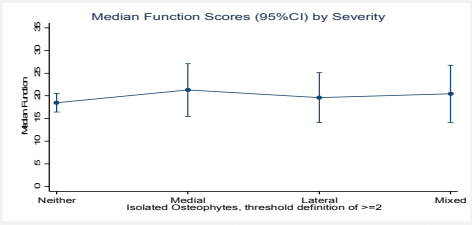
**OSTEOPHYTES**

**Threshold Grade ≥1**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median function score (95%CI)** | 18.1 (15.5, 20.7) | 19.9 (15.6, 24.2) | 18.6 (15.5, 21.7) | 21.2 (18.5, 23.8) |
| **Median difference (95%CI)** | Ref | 1.8 (-3.2, 6.8) | 0.5 (-3.6, 4.7) | 3.1 (-1.0, 7.2) |
| **P value** | - | P=0.474 | P=0.803 | P=0.142 |

**Threshold Grade ≥2**




| | Neither | Isolated medial | Isolated lateral | Mixed |
|---|---|---|---|---|
| **Median function score (95%CI)** | 18.5 (16.4, 20.5) | 21.3 (15.5, 27.1) | 19.6 (14.1, 25.1) | 20.4 (14.1, 26.8) |
| **Median difference (95%CI)** | Ref | 2.8 (-3.5, 9.1) | 1.2 (-5.1, 7.4) | 2.0 (5.0, 9.0) |
| **P value** | - | P=0.384 | P=0.716 | P=0.584 |

**Supplementary Data Table S1. Summary of studies reporting relative frequency of medial vs. lateral PFJOA**

| | **Gross et al 2012** | **Ratzlaff et al 2014** | **Hayashi et al 2014** | **Iwano et al 1990** | **Elahi et al 2000** | **Cahue et al 2004** | **Crossley et al 2012** |
|---|---|---|---|---|---|---|---|
| Study type | Cross sectional | Cross sectional | Cross sectional | Cross sectional | Cross sectional | Longitudinal | Cross sectional |
| Imaging modality | MRI | MRI | MRI | X-ray, skyline view with knee flexion of 45° | X-ray, skyline view with knee flexion of 30° | X-ray, skyline view with knee flexion of 30° | X-ray, skyline view with knee flexion between 30 - 40° |
| OA Definition | WORMS - Cartilage morphology only: Applied four different cut-offs ≥2, ≥3, ≥4 and ≥5 | Automated BML volume: assessed continuously | WORMS OP Grade ≥2 and Cartilage morphology: (Grade ≥2 reported separately | Knees with ALL three features – osteophytes, JSN and subchondral sclerosis, PLUS JSN < 3mm | OARSI atlas – asymmetric PF JSN and presence of PF OP | OARSI atlas - PF JSN: an increase grade ≥1 indicated progression | Kellgren Lawrence grade: Described frequencies in mild and moderate/severe groups. |
| Population/Participants description | BOKS – adult symptomatic knee OA cohort<br><br>FOA – adult population-based cohort, no selection based on the presence/ absence of knee OA<br><br>MOST – adults with existing knee OA or at high risk of developing the disease | Osteoarthritis Initiative Progression Cohort – Adults with definite knee OA | Framingham Community Cohort – radiographically 'normal' knees i.e. no ROA; though used only lateral x-ray views and no skyline views | Adults with definite knee OA (Japanese population) – knees with moderate to severe OA | Adults with definite symptomatic knee OA | Adults with definite symptomatic knee OA | Baseline RCT sample – individuals with chronic anterior knee pain |
| Mean age (SD), years | BOKS 66.7(9.4);<br><br>FOA 65(8.9)<br><br>MOST 62.1(8.0) | - | 62.3(8.4) | 62.6 | 66 (11) | 68.4(10.8) | 54 (10) |
| Sex (Female) | BOKS 41.1%<br><br>FOA 56%<br><br>MOST 61% | 48% | 55.2% | 92.4% | 71% | 71% | 51% |
| BMI (SD), kg/m$^2$ | BOKS 30.7(4.8)<br><br>FOA 29.2(5.5)<br><br>BMI 30(4.9) | - | 27.9(5.1) | - | 31(7) | 30.6(6.1) | 27(4) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Findings | Medial PFJOA more prevalent than lateral, except at higher OA definition cut-offs where lateral PFJOA prevalence approximated (and slightly exceeded) that of medial PFJOA. Finding consistent across all three study populations. | Prevalence: medial – 46%, lateral – 44%.<br><br>PFJ BML at least as common medially as laterally | Prevalence of pre-radiographic OA changes - Cartilage morphology: medial 47.7%, lateral 29.9%<br><br>Osteophytes: medial 24.6%, lateral 34% | Lateral PFJOA was more common than medial PFJOA | Lateral PFJOA was more common than medial PFJOA; knees with PFJOA were more often valgus than knees with isolated TFJOA | Lateral PFJOA progression was more common than medial PFJOA progression | Prevalence of medial and lateral PFJOA appear equal |

WORMS – whole organ magnetic resonance imaging score, BML – bone marrow lesion, JSN – joint space narrowing, OP – osteophytes, PFJOA – patellofemoral joint osteoarthritis, PF patellofemoral